REMARKS

Claims 3, 9, 10, and 18-22 are pending in the present application.

The rejections of: (a) Claims 3, 18, and 22 under 35 U.S.C. §102(e) over Himmelspach et al, (b) Claims 19-21 under 35 U.S.C. §103(a) over Himmelspach et al, and (c) Claims 9-10 under 35 U.S.C. §103(a) over Himmelspach et al, are respectfully traversed.

Independent Claim 3 is drawn to a factor X analogue having the sequence Leu-Thr-Arg-Ile-Val-Gly (SEQ ID NO: 1) of the activation site of native factor X replaced with the sequence Val-Pro-Arg-Ala-Val-Gly (SEQ ID NO: 9). Applicants respectfully submit that Himmelspach et al fails to disclose or suggest this specific mutation with sufficient particularity to support an anticipation and/or obviousness rejection.

Himmelspach et al disclose Factor X analogues having the generic sequence:

GIy228-R6-R5-R4-R3-R2-Arg234-R I,

wherein:

a) R1 is an amino acid selected from the group consisting of Ile, Val, Ser, Thr, and Ala,

b) R2 is an amino acid selected from the group consisting of Pro, Gly, Lys, and Arg,

c) R3 is an amino acid selected from the group consisting of Phe, Lys, Met, Gin, Glu, Ser, Val, Arg, and Pro

d) R4 is an amino acid selected from the group consisting of Asp, Ile, Ser, Met, Pro, Thr, Arg, Lys,

e) R5 is an amino acid selected from the group consisting of Asn, Lys, Ser, Glu, Ala, Gln, His, and Arg, and

f) R6 is an amino acid selected from the group consisting of Asp, Phe, Thr, Arg, Leu, and Ser.

Himmelspach et al fail to disclose or suggest a factor X analogue having the sequence Leu-Thr-Arg-Ile-Val-Gly (SEQ ID NO: 1) of the activation site of native factor X replaced with the sequence Val-Pro-Arg-Ala-Val-Gly (SEQ ID NO: 9) with sufficient specificity and

the artisan would have no reason to select this factor X analogue from the extensive list of alternative factor X analogues, much less an expectation of the beneficial results flowing from the same.

Indeed, when a compound is not specifically named, but instead it is necessary to select portions of teachings within a reference and combine them, as in Himmelspach et al, anticipation can only be found if the classes of [possibilities] are sufficiently limited or well delineated. *Ex parte A*, 17 USPQ2d 1716 (Bd. Pat. App. & Inter. 1990). If one of ordinary skill in the art is able to "at once envisage" the specific compound within the generic chemical formula, the compound is anticipated. Typically, one of ordinary skill in the art must be able to draw the structural formula or write the name of each of the compounds (or in this case, each factor X analogue) included in the generic formula before any of the compounds can be "at once envisaged." One may look to the preferred embodiments to determine which compounds can be anticipated. *In re Petering*, 301 F.2d 676, 133 USPQ 275 (CCPA 1962). However, at no point is a factor X analogue having the sequence Leu-Thr-Arg-Ile-Val-Gly (SEQ ID NO: 1) of the activation site of native factor X replaced with the sequence Val-Pro-Arg-Ala-Val-Gly (SEQ ID NO: 9) specifically disclosed or exemplified in Himmelspach et al. Further, the generic formula define in Himmelspach et al that the Examiner alleges embraces the claimed factor X analogue literally embraces thousands of alternative peptides.

The breadth of the scope of compounds embraced by Himmelspach et al is important to the analysis of whether the artisan would envision any one specific, unnamed compound. In *In re Petering*, the prior art disclosed a generic chemical formula that possessed a generic class consisting of about 20 compounds. This decision represents the minimum threshold (one in 20) to hold that a reference "described" the claimed compound such that one of

ordinary skill in the art is able to "at once envisage" the compound. As such, when the generic class consists of 20 or less compounds the reference is generally taken to anticipate the claims. However, where the generic class exceeds 20, then *at best* it should be more properly treated as an obviousness rejection. Thus, Applicants submit that the Examiner's anticipation rejection is without merit and should be withdrawn. Applicants further submit that Himmelspach et al do not support even an obviousness rejection.

When looking to see whether there would even be a motivation to select the specifically claimed factor X analogue, the artisan may look to the preferred analogues disclosed by Himmelspach et al. However, Himmelspach et al disclose that the more preferred analogues correspond to particular combinations of substituents represented by SEQ ID NOs: 29-74. Notably, none of these preferred analogues comprises the specific combination wherein R1 would be Ala, R2 would be Pro, and R3 would be Val, which corresponds to the Factor X analogue of the presently claimed invention.

Indeed, the analogues more specifically disclosed by Himmelspach et al do not include any analogue wherein R1 is Ala. It is further noted that in the analogues wherein R2 is Pro (SEQ ID NOs: 32-35), R1 is *always* Ile, and R3 is *always* Lys. Further, in the analogues wherein R3 is Val (SEQ ID NOs: 54-61 and SEQ ID NO: 73), R1 is *always* Ile, and R2 is either Arg (SEQ ID NOs: 58-61) or Thr (SEQ ID NOs: 54-57 and SEQ ID NO: 73).

Accordingly, Himmelspach et al at best provides a generic disclosure, which cannot be considered as anticipating the particular combination of substituents which characterizes the factor X analogue of the claimed invention. Himmelspach et al also fail to provide any reasonable basis to select or arrive at the claimed factor X analogue.

Moreover, Applicants further submit that Himmelspach et al do not disclose any Factor Xa analogue resulting from the cleavage of Factor X analogue of the claimed invention. Therefore, Himmelspach et al can not anticipate claim 18.

Applicants also submit that although Himmelspach et al disclose that for optimal processing, it may be necessary in individual cases to exchange the amino acid Ile235 (the N-terminal amino acid in native Factor Xa) and describes Factor X analogues wherein IIe235 is exchanged for Val or Ser, it also specifies that preferably the N-terminal Ile should still be present after activation, since it plays an essential part in the catalytic mechanism of factor Xa (column 5 lines 41-48). Himmelspach et al is silent about the procoagulant properties of Factor Xa analogues wherein the N-terminal amino acid is Val or Ser.

In the present application, see in particular Example 6 and Table XI, Applicants have demonstrated that while a Factor Xa analogue (SVG) wherein the N-terminal amino acid is Ser (i.e a Factor Xa analogue which may result from activation of a Factor X analogue of Himmelspach et al wherein R1 is Ser) is devoid of detectable procoagulant activity, the Factor Xa analogue of the present invention (AVG) wherein the N-terminal amino acid is Ala has a procoagulant activity which is comparable to the one of native Factor Xa.

These properties of the Factor Xa analogue of the present invention are not disclosed and would not have been expected in view of the disclosure of Himmelspach et al. Specifically, Himmelspach et al do not even mention Ala among the preferred R1 substituents. Thus, the artisan would have no way to expect the advantages of the present invention.

In view of the foregoing, Applicants submit that not only do Himmelspach et al fail to disclose, but also fail to suggest the subject matter of Claims 3, 18 and 22. Indeed, since the Factor X and Factor Xa analogues analogue of the instant invention are not disclosed in

Himmelspach et al with sufficient specificity to support an anticipation and/or obviousness rejection for the reasons above, one of skill in the art would also not find any motivation in Himmelspach et al to prepare nucleic acid molecules, expression vectors, and host cells that can be used to express these analogues or to use said analogues to treat blood coagulation disorders. Accordingly, Claims 9-10 and 19-21 would also not be obvious in view of Himmelspach et al.

Withdrawal of these grounds of rejection is requested.

Applicants respectfully submit that the above-identified application is now in condition for allowance. Early notification to this effect is earnestly solicited.

Respectfully submitted,

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